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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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08/462,703

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GARY D. HODGEN

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EXAMINER

SULLIVAN, DANIELLE D

ART UNIT

PAPER NUMBER

1616

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 08/462,703	Applicant(s) HODGEN ET AL.	
	Examiner DANIELLE SULLIVAN	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 December 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 42-44, 56-76, 82, 83, 86-105, 108, 110, 112-117 and 119-134 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 42-44, 56-76, 82, 83, 86-105, 108, 110, 112-117 and 119-134 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>05/05/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Prosecution has been reopened. Claims 42-44, 56-76, 82, 83, 86-105, 108, 110, 112-117 and 119-134 are pending. The examiner for this application has changed from Edward Webman to Danielle Sullivan who can be reached at 571-270-3285.

Withdrawn rejections

Any rejection and/or objection not specifically addressed below are herein withdrawn.

Double Patenting

Claims 56-58 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 42-44. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 67-71 and 72-76 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 56-60. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 42-44, 82, 84-92, 102-105 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 54-56, 94, 96-101, 103, 48-51 of copending Application No. 08/115008 in view of Casper (US 5,108,995). Although the conflicting claims are not identical, they are not patentably distinct from each other. The copending claims relate to a method of contraception whereas the present claims relate to a hormone replacement therapy.

Casper teaches that methods of contraception which employ a combination of estrogen and progestin or also employed in the treatment for hormonal replacement therapy for menopausal women and that contraception is a form of hormone therapy (column 1, lines 7-15). Therefore, it would have been prima facie obvious to one of ordinary skill in the art to use a method of contraception to treat postmenopausal women in need of hormone replacement therapy.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 61-66 and 127 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 66, the dose of 50-500 mg is indefinite because the method requires dosage in 1-10 mg/kg and the weight of the patient is unknown. Therefore, the limitation of the dosage in mg and mg/kg are not understood.

Claim 127 recites the limitation "period of antiprogesterin administration ". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 42-44, 56-76, 82, 83, 86-101, 108, 110, 112-117 and 119-127 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ortmann et al. (Inhibitory Effects of the Antiprogesterin, RU 486, 1989) in view of Casper (US 5,108,995).

Applicant claims a method of hormone replacement therapy comprising administering to a woman an effective amount of estrogen in combination with an effective amount of a progestin, and an amount of antiprogesterin effective to ameliorate uterine bleeding problems, eg. breakthrough bleeding and withdrawal amenorrhea. In the method, the antiprogesterin is administered periodically or continuously, whereas the estrogen is administered continuously. Preferably, the antiprogesterin is equivalent to an oral dose of about 1-10 mg/kg.

Applicants also claim a method where the estrogen (preferably, ethinyl estradiol or an ester thereof 0.005-0.015 mg/day mestranol 0.020-0.025 mg/day or conjugated estrogens 0.005-0.015 mg/day) is administered daily with progestin (preferably, gestodene or norethindrone acetate), at intervals of at least about a month, administering an antiprogestin (such as, mifepristone). Preferably, the dosage is taken orally and give to a female that is para- or post menopausal.

Ortmann et al. teaches RU-486 (mifepristone) combined in treatment with estradiol and progesterone. The inhibitory effect of RU-486 is enhanced in the presence of estrogen and antiprogestin is also a potent antagonist of both the inhibitory and facilitatory actions of progesterone and therefore is an effective progestin agonist (abstract). RU-486 is taught as a contraceptive, which causes uterine lining shedding and induces menstrual bleeding during the luteal phase of the cycle (page 291, column 1, paragraph 1). Ortmann et al. does not teach continuous administration of estrogen. Neither are specific dosages, progestins (synthetic progesterones) such as, gestodene, norethindrone or estrogens such as, ethinyl estradiol, mestranol taught. It is for this reason that Casper is joined.

Casper teaches that hormone replacement therapy with continuous (daily or cyclic) estrogen in combination with a progestin regimen for hormonal replacement avoids the problem of withdrawal bleeding in menopausal women (column 5, lines 40-49 and 66 thru column 6, line 1). Casper teaches that daily administration of a progestin results in endometrial atrophy which may be associated with breakthrough bleeding (column 6, lines 5-8). The synthetic estrogens can be selected from ethinyl

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estradiol, mestranol and conjugated estrogens, while progestin may be selected from gestoden and norethindrone acetate (column 8, lines 39, 40, 48-61). The dosage are as follows: estrogen 0.02-0.05 mg and progestin 0-1 mg (column 9, lines 23-31).

It would have been obvious to combine Ortmann et al. and Casper to include a method of hormone replacement therapy comprising administration of estrogen, a progestin and an antiprogestin. One would have been motivated to combine an antiprogestin because it is a contragestive and would induce scheduled bleeding during the luteal phase of the cycle as taught by Ortmann et al. and therefore reduce the incidence of breakthrough bleeding. Furthermore, it would act as a progestin agonist and reduce the development of endometrial atrophy caused by the administration of progestin as taught by Casper.

It would have been obvious to combine Ortmann et al. and Casper to include the specific dosages in the range of or estrogens near 0.02-0.05 for this is routine optimization and is dependent on the particular womans needs. Furthermore, it is routine optimization to adjust whether the antiprogestin is administered periodically or continuously while the estrogen is administered continuously. Since menopausal women do not have regular cycles and eventually stop having uterine bleeding, the patient would not need cyclic or continuous use of the antiprogestin. However, estrogen and progestin administration can be continued without interruption as taught by Casper since breakthrough bleeding would no longer be an issue.

Furthermore, it would have been obvious to combine the teachings of Ortmann et al. and Casper to include the progestins gestodene and norethindrone and the

estrogens ethinyl estradiol and mestranol. One would have been motivated to include these progestins and estrogens because they are commonly used in hormone replacement therapy.

Claims 102-105 and 128-134 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ortmann et al. (Inhibitory Effects of the Antiprogestin, RU 486, 1989) in view of Casper (US 5,108,995).

Applicant teaches kit comprising at least 20 estrogen and progestin-containing tablets and an amount of antiprogestin to induce menses. Preferably, the kit contains 28 estrogen and progestin tablets arranged to be taken sequentially with the antiprogestin tablet positioned as the 20th or later tablet in the sequence and are used in the method as addressed in above 103 rejection.

Ortmann et al. teaches the method as addressed in above 103 rejection. Ortmann et al. does not teach a kit. It is for this reason that Casper is joined.

Casper teaches oral contraceptives and hormone replacement therapies as addressed in the above 103 rejection. The dosages may be formulated into a pharmaceutical kit or package with daily dosages arranged for proper sequential administration (column 10, lines 36-45)

It is well-settled law that combining printed instructions and an old product into a kit will not render the claimed invention nonobvious even if the instructions detail a new use for the product. See *In re Ngai*, 367 F.3d 1336, 1339, 70 USPQ2d 1862, 1864 (Fed. Cir. 2004). Further, the inclusion of a package insert or label showing the "the name of

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drug, dosage, dosage form, route of administration, indication and direction of use" of a pharmaceutical composition is mandated by 21 CFR 201.57 and is therefore obvious to one of ordinary skill in the art.

Therefore, it would have been obvious to combine the teachings of Ortmann et al. and Casper to include a kit comprising a set amount of dosages. One would have been motivated to formulate the dosages into a kit in order assured that the method is taken in sequential order as taught by Casper.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. State of the Art: Wood (Mifepristone (RU 486)-A Modulator of Progestin and Glucocorticoid Action, 1993).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Danielle Sullivan whose telephone number is (571) 270-3285. The examiner can normally be reached on 7:30 AM - 5:00 PM Mon-Thur EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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